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## THE INFLUENCE OF THE NERVE ON THE REGENERATION OF THE LEG OF *DIEMYCTYLUS*.

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The following experiments were carried on at the suggestion of Professor Morgan, for the purpose of ascertaining whether regeneration in the leg of *Diemyctylus* is dependent on its connection with the nervous system, as has been found in the case of other urodeles, or whether the supposed result may not have been due to unintentional injury to the blood supply. The hind limb was chosen for operating on account of its larger size. The general course of procedure was to cut the nerve in the upper part of the leg *without injury to the artery*, and then amputate the leg at the knee joint. After a period of a little more than three weeks the new part can be clearly recognized as a dark protuberance sharply contrasting with the lighter color of the surrounding skin.

In the first lots the nerve was cut as near the proximal end of the femur as possible. A longitudinal slit through the skin was made with a sharp knife. The muscles were then separated until the nerve was brought into view. Care was taken not to injure the blood vessel which closely adheres to the nerve and is almost inseparable from it. If the operation were performed without injury to the blood vessel and the leg showed a resulting paralysis it was amputated at the knee. For comparison an equal number of salamanders had the leg cut off without injuring the nerve or blood vessel. The results obtained from the first series seemed to show that regeneration in *Diemyctylus* was in no way dependent upon the nerve. The proliferation of new material began as soon in those in which the nerve had been cut as it did in the checks. Nor did the amount of material regenerated seem to be affected in any way. There were, it is true, great variations in the rate of regeneration, but these seemed to arise from purely individual differences, and to bear no definite relation to the presence or absence of the nerve connection. In two checks operated upon on the same day and kept in the same

aquarium, so that external conditions could play little, if any, part in the result, an interval of ten days or more might occur between the earliest and latest appearance of proliferation. The results obtained after cutting the nerve at this level may have been due to the presence of collateral nerve-connection sufficient to give the required stimulus to the tissue ; for as was later clearly shown, the nerve is an important factor in the regeneration.

In the succeeding series the nerve was cut through the pelvic girdle close to the backbone, in the hope of more completely cutting off the nerve supply of the limb. The incision necessarily went through into the body cavity as the nerves given off from the spinal cord lie close to the inner wall and are covered only by cœlomic epithelium. The operation is by no means as serious as would be imagined, since the wound heals completely in three days. During this time the animal acts in a perfectly normal manner except for the injured leg. Instead of using separate individuals for checks as before, both legs of the same individual were amputated, but the nerve was cut on one side only. The males are much more difficult to operate upon than the females, on account of their greater muscular development, whereas in the female the pelvic girdle stands out prominently and the body wall is thin. In the males the girdle is not visible externally and is overlaid by a thick musculature which renders operating upon the animal at this point difficult.

On November 26 a set of seven salamanders was operated upon as described above. They were not again observed until the forty-fifth day. At that time both legs of each individual had proliferated material to a greater or less extent. The side used as a check could be identified in every case but one, by its far greater amount of proliferated material.

In the exception the animal assumed a peculiar green color, evidently from a disease, and at a later period both legs were entirely sloughed off. This set was continued under observation until the eighty-third day, at which time there was still a decided difference between the appearance of the two sides, although by no means as pronounced as before. The check showed in each individual the foot plainly differentiated, while in only two instances was this the case upon the other side, and even in those cases to a much less extent.

Later I operated upon at least thirty salamanders in several lots. Some of these were starved while others were well fed. The abundance or lack of food did not seem to be a factor in the rate of regeneration. Salamanders which were reduced almost to "skin and bones" showed the same comparative amount of regeneration as well-fed individuals. The influence of food did show itself, however, in the amount of material proliferated. During starvation an individual shrinks greatly in size and proliferates much less material for the same relative amount of regeneration as a well-fed companion.

To ascertain whether the blood supply was a factor in regeneration the artery of several individuals was cut just above its entrance into the leg, the nerve being left intact. The result showed that the leg regenerated at the normal rate. However, not much stress can be laid upon this experiment, owing to the rapidity with which a sectioned blood-vessel heals.

That the circulation in the leg may have continued to some extent after the operation in those individuals whose nerve as well as artery had been sectioned near the backbone was shown conclusively by the following experiment. A salamander was taken and a cut made in the pelvic region as before. Then a vein was severed in the lower part of the leg. This continued to bleed freely for a considerable time, as would not have occurred had the total blood supply been cut off. The collateral blood supply probably still brought blood to the limb. Similarly the collateral nerve supply may in the first series of experiments have sufficed to keep the regeneration up to the same rate as in a limb in which the nerve was not cut.

In a number of cases regeneration did not set in at all on the side on which the nerve had been cut. At least, after a period of two months and a half there was not the least sign of proliferation, while in the normal course of regeneration the new part appears in about twenty-five days. This lack of regeneration is probably due to the distal end of the nerve being displaced, and in consequence the regenerating nerve was unable to grow down its old path along the degenerated nerve, but was turned aside. Consequently not even a retarded regeneration occurred.

The most important work bearing on the question of the rela-

tion between the nerve and the regeneration of the leg is that of Wolff.<sup>1</sup> He found that if the nerve-cord were destroyed in the region of origin of the leg nerve that the leg regenerated at the normal rate. Since the spinal ganglion was left after this operation, its presence may have sufficed to produce the result. In fact, nerves were found in the new foot. In order to remove the ganglion also, a piece of the spinal column was cut out including cord and ganglion. Six individuals that survived this operation showed that after the first proliferation of new material had taken place growth came to a standstill for a time and then began again. The result suggests, Wolff thinks, that the standstill was due to the lack of nerve connection, while the renewal of growth was due to the reestablishing of a new nerve connection. In fact the disabled leg showed some signs of having regained its power of motion.

Wolff discusses the question whether the period of standstill may not have been due to the lack of function or activity of the leg while its later growth was due to its regaining its locomotor function. He argues that this is probably not the case, but that the nerve connection is directly responsible for the result.

A student of Busfurth's, R. Rubin,<sup>2</sup> has obtained similar results. What part the nervous connection plays in these cases is still obscure. Morgan and Davis<sup>3</sup> have found that for the regeneration of the tail of the tadpole, the presence of the notochord and not the nervous system is the important factor.

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<sup>1</sup> *Virchow's Archiv*, CLXIX., 1902.

<sup>2</sup> *Archiv Entw. Mech.*, XVI., 1903.

<sup>3</sup> *Archiv Entw. Mech.*, XV., 1903.